UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/507,267 | 04/06/2005 | Eugeny A. Lukhtanov | 17682-005010US | 4902 |

20350 7590 08/16/2007

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

| EXAMINER | |
|---|---|
| STAPLES, MARK | |
| **ART UNIT** | **PAPER NUMBER** |
| 1637 | |
| **MAIL DATE** | **DELIVERY MODE** |
| 08/16/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/507,267 | LUKHTANOV ET AL. | |
| | Examiner | Art Unit | |
| | Mark Staples | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *3, 7-9, 21-23, 26, 29,33-56, and 58-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4- 6, 10-20, 24, 25, 27-28, 30-32 and 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 September 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

## ETAILED ACTION

### *Election/Restrictions*

1. Applicant's election with traverse of Group I and species as presented in the reply filed on 07/20/2007 is acknowledged. The traversal is on the ground(s) that the structure of species are related to each other by design. This is not found persuasive because there are a multitude of different structures which creates an enormous search burden as the search of any one structure is not co-extensive with the search of any other structure.

The requirement is still deemed proper and is therefore made FINAL.

Claims reading on the elected species are claims 1, 2, 4- 6, 10-20, 24, 25, 27-28, 30-32 and 57.

Claims 3, 7-9, 21-23, 26, 29, 38-56, and 58-63 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/20/2007.

Claims 1, 2, 4- 6, 10-20, 24, 25, 27-28, 30-32 and 57 are pending and at issue.

### *Specification*

2. The use of the trademarks OREGON GREEN™, RIBOGREEN™, RHODAMINE GREEN™, and MAGNESIUM GREEN™ have been noted in this application. They and

any other trademarks should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is advised to scan the entire application to ensure trademarks usage in all the places where it appears in the application is in compliance with the current office guidelines.

***Sequence Rules Compliance***

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is given time of reply to this office action within which to comply with the sequence rules, 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in **abandonment** of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the

undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Page 65 contains sequences without SEQ ID NOs. If these sequences are included in the sequence listing provide by Applicant, the specification should be amended to include the SEQ ID NOs. If these sequences were not filed, Applicant should provide a sequence listing and a CRF that include those sequences.

***Double Patenting***

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 2, 4- 6, 10-20, 24, 25, 27-28, 30-32 and 57 are rejected on the ground of nonstatutory double patenting over claims 1-34 of U. S. Patent No. 6,790,945 since

the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: the structures of the instant claims are encompassed by the structures in the patent claims. The instant claims use the language of "a negatively charged minor groove moiety" as part of conjugated compound and such a moiety is found within the patent compounds as disclosed in columns 69 and 70 with the negatively charged groups listed in column 69 lines 56 and 57 which are part of the minor groove moiety. The patent claims encompass these negatively charged groups/moieties. The patent also discloses the use of the compounds in pharmaceutical compositions, that is, as drugs and toxins (see column 11 lines 11-16).

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 2, 4, 5, 10-20, 24, 25, 27-28, 30-32 and 57 are rejected under 35 U.S.C. 102(e) as being anticipated by Lukhtanov et al. (US Patent No. 6,790,945 filed June 6, 2001).

Regarding claims 1, 2, 4, 5, 10-13, Lukhtanov et al. teach an oligonucleotide-negatively charged minor groove binder conjugate comprising:

a negatively charged minor groove binder moiety comprising:

a plurality of three aryl moieties (each moiety having an aryl benzyl ring in the structure found in columns 69 and 70) and

at least one acidic moiety capable of ionizing under physiological conditions, wherein said acidic moiety is covalently attached to at least one of said aryl moiety (see the structure found in columns 69 and 70, and column 69 lines 55-58 where the acidic moieties can be ...-$SO_3^-$, ...-$PO_3^-$, and ...-$CO_2^-$); and

an oligonucleotide moiety which is covalently attached to said negatively charged minor groove binder moiety (entire patent, especially the structure found in columns 69 and 70; and see claims 1-10).

Regarding claim 6, Lukhtanov et al. teach where the oligonucleotide comprises from about 3 to about 100 nucleotide units (see column 68 line 28).

Regarding claims 14 and 15, Lukhtanov et al. teach covalently bound quenchers through linkers (see claims 1-11).

Regarding claim 16, Lukhtanov et al. teach: ". . . non-fluorescent quencher dyes including the dabcyl (. . . absorbance max=453 nm)" (see column 2 lines 20-22).

Regarding claim 17, Lukhtanov et al. teach covalently bound fluorophores through linkers (see claims 1-11).

Regarding claim 18, 27, and 28, Lukhtanov et al. teach where fluorescent emission maximum is between about 400 and 900 nm (see column 11 lines 58-60) and teach where the fluorophore is fluorescein (see column 2 line 55).

Regarding claims 19 and 20 and the elected species, Lukhtanov et al. teach the conjugate and NMGB structures given (see structure in column 4 lines 35-40; see NMGB structures found in columns 69 and 70; and see column 69 lines 55-58 where the acidic moieties can be ...-$SO_3^-$, ...-$PO_3^-$, and ...-$CO_2^-$);

Regarding claims 24 and 25 and the elected species, Lukhtanov et al. teach the quencher structure (see column 15 lines 21-32).

Regarding claim 30 and the elected species, Lukhtanov et al. teach the moiety structure given (see Table 4 found at column 77).

Regarding claim 30 and 32, Lukhtanov et al. teach the formula given by teaching the compoents as noted above and teaching how they can be combined into the structure given (see structure in column 4 lines 35-40).

Regarding claim 57, Lukhtanov et al. teach the use of the compounds in pharmaceutical compositions, that is, as drugs and toxins (see column 11 lines 11-16).

8. Claims 1, 2, 6, 10, 11, 13, 14 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by Sinyakov et al. (March 2001, cited in previous Office Action, which is an English translation of the original Russian article published on February 26, 2001 in Molekulyarnaya Biologiya, Vol. 35, No. 2, 2001).

Regarding claims 1, 2, 6, 10, 11, and 13, Sinyakov et al. teach an oligonucleotide-negatively charged minor groove binder conjugate comprising:
a negatively charged minor groove binder moiety comprising:
at least one aryl moiety (see Figure 2 for the heteroaryl aminopyrrole of MGB-4) and
at least one acidic moiety capable of ionizing under physiological conditions, wherein said acidic moiety is covalently attached to at least one of said aryl moiety (see Figure 2 for the carboxylic acid of MGB-4); and
an oligonucleotide moiety which is covalently attached to said negatively charged minor groove binder moiety (entire article, especially the Title, and the 5$^{th}$ sentence of the Abstract: "The best stabilizers of a triplex were novel conjugates in which two parallel molecules containing six pyrrole units each are linked to the same 5'-phosphate of a 16-mer triplex-forming oligonucleotide").

Regarding claim 14, Sinyakov et al. teach where ". . . a linker between the oligonucleotide and the ligand, hexamethylenediamine was used" (see 1$^{st}$ sentence on p. 256).

Regarding claim 57, Sinyakov et al. teach a pharmaceutical composition of the oligonucleotide charged minor groove binder as follows: "The discovery of synthetic ligands recognizing certain DNA sequences . . . and of triplex-specific intercalators . . .

considerably raised the chances of creating addressed reagents [pharmaceutical compositions]. One of the most promising directions toward their construction is covalent conjugation of ligands to oligonucleotides. First, the conjugate recognizes a longer sequence of target DNA and the stability of the resulting complexes increases. Second, the enhanced complementarity of the conjugate to its target allows the effective concentrations of the agent to be considerably reduced, which is important for the potentially toxic compounds. Third, the covalent attachment to oligonucleotides makes water soluble quite hydrophobic ligands, which are hard to use in a free state. The efficiency of this approach was demonstrated in a number of papers on the stabilization of double and triple helices [references cited] " (see 2nd paragraph on p. 251).

***Reference of Interest***

Bailley (2000, cited in previous Office Action) is made a reference of interest. Bailley teaches a negatively charged minor groove binder compound/moiety with an acidic sulphate ester attached to an aryl moiety (see see structure UCE 1022 in Figure 11).

***Conclusion***

9. No claim is free of the prior art.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-

9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 7:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples MS
Examiner
Art Unit 1637
August 14, 2007

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
8/14/07

| Notice to Comply | Application No. 10/507,267 | Applicant(s) LUKHTANOV ET AL. | |
|---|---|---|---|
| | Examiner Mark Staples | Art Unit 1637 | |

## NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e). The correct SEQ ID NO:2 is present in the paper copy of the of the sequence listing only. Therefore a search of the correct sequence is not possible.

☒ 7. Other: See Office Action.

### Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

**PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY**